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Cutaneous Reactions Following Booster Dose Administration of COVID-19 mRNA Vaccine: a first look from the AAD/ILDS Registry

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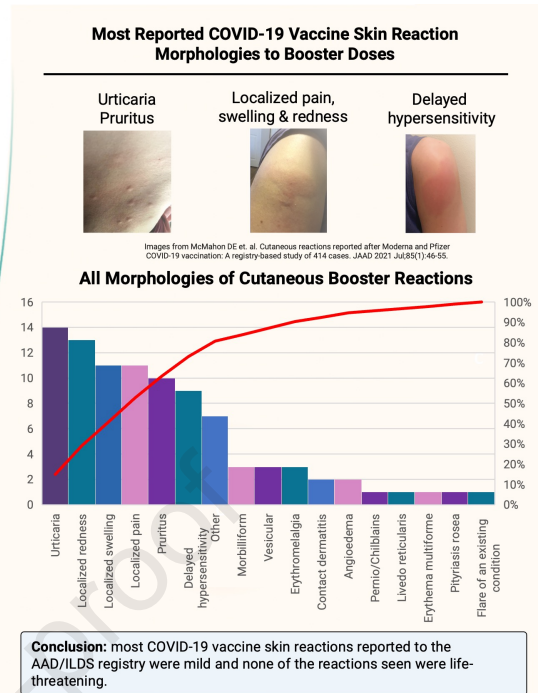
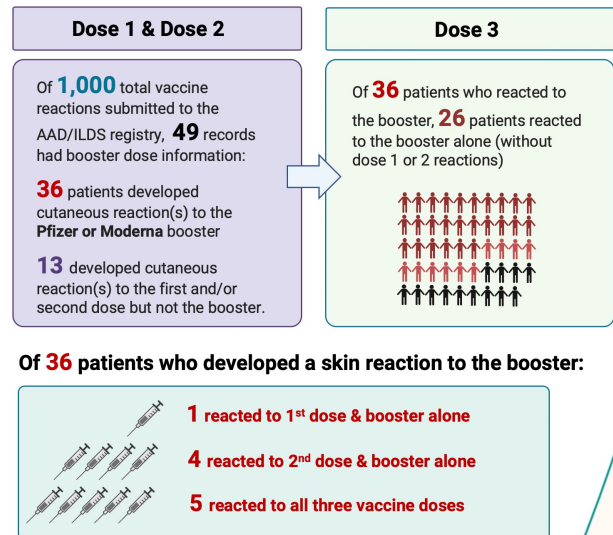


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Cutaneous Reactions Following Booster Dose Administration of COVID-19 mRNA Vaccine: a first look from the AAD/ILDS Registry



Article type: Research Letter

Title: Cutaneous Reactions Following Booster Dose Administration of COVID-19 mRNA Vaccine: a first look from the AAD/ILDS Registry

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Conflicts of Interest: Drs Freeman, Hruza, Rosenbach and Fox are members of the American Academy of Dermatology (AAD) COVID-19 Ad Hoc Task Force. Dr Freeman is an Editor for the BJD. Dr French is the President and Dr Lim is a board member of the International League of Dermatological Societies. Dr Freeman is an author of COVID-19 dermatology for UpToDate. Dr Blumenthal and authors Prasad, Ali, Singh and Tyagi have no conflicts of interest to declare.

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Booster doses for the COVID-19 mRNA vaccine ≥ 6 months after completion of a patient's primary vaccine series are now in use across the globe (1,2). While cutaneous vaccine reactions have been widely reported in response to the original series of mRNA vaccines (3-5), little is known about adverse cutaneous reactions to booster administration. We sought to evaluate cutaneous side effects after mRNA COVID-19 booster to (1) describe reaction sequences after first, second and booster doses, and (2) characterize cutaneous reaction morphology following vaccine booster administration.

The American Academy of Dermatology (AAD) and International League of Dermatologic Societies (ILDS) COVID-19 Dermatology registry was established in April 2020 for SARS-CoV-2 skin manifestations; vaccine reactions were added in December 2020. In September 2021, the registry was adapted to include COVID-19 vaccine booster reactions as either new cases or updates to existing registry entries. Case entry was open to health professionals only; data reported to the registry were deidentified.

From Dec 24, 2020 to January 23rd, 2022, 1,000 individual cases of COVID-19 vaccine cutaneous reactions were entered into the registry, of which 49 records included data about the presence or absence of a cutaneous reaction following booster administration. Of 49 records, 36 patients (73%) developed cutaneous reaction(s) to the booster and 13 (27%) developed cutaneous reaction(s) to the first and/or second dose but not the booster. Of the 36 patients who developed a cutaneous reaction to the booster, 26 reacted to the booster alone, 1 reacted to the first and booster alone, 4 reacted to the second and booster alone, and 5 reacted to all three vaccine doses.

Among the 36 individuals with booster reactions, a total of 93 distinct cutaneous reactions were reported, primarily to Moderna (n=63) or Pfizer (n=20) mRNA vaccines. The most common morphologies among all booster cutaneous reactions were urticaria (n=14), local injection site reactions [swelling (n=11), redness (n=13), and pain (n=11)], delayed large local reaction (n=9), erythromelalgia (n=3), and vesicular reactions (n=3) (**Table 1**). Only one patient who originally received the Pfizer series and switched to a Moderna booster had a booster reaction, and one patient who originally received the Moderna series then received a Pfizer booster had a booster reaction. There were no reported booster reactions in patients who had Johnson & Johnson for their original vaccine series who then switched to an mRNA vaccine for their booster dose.

Of all COVID vaccine reaction cases in the AAD/ILDS registry, booster reactions only represent a small portion. Several reasons may exist for relatively infrequent reporting: physicians may not have seen the patient in follow-up, reporter fatigue, slow uptake of boosters, and/or booster reactions may truly be less frequent than reactions to doses 1&2. Dermatologists should be aware that cutaneous reactions to booster shots are possible, even when reactions to dose 1 and 2 did not occur. Even with a bias towards reporting notable reactions, most reactions were mild and none of the reactions seen were life-threatening. This data provides additional reassurance on the safety profile of booster vaccines.

References

1. Times of Israel. Israel becomes first country in the world to give COVID boosters to over-50s. Available at: <https://www.timesofisrael.com/israel-becomes-first-country-in-world-to-offer-covid-boosters-to-over-50s/> (last accessed 20 January 2021).

2. U.S. Food and Drug Administration. FDA authorizes booster dose of Pfizer-BioNTech COVID-19 Vaccine for Certain Populations. Available at: <https://www.fda.gov/news-events/press-announcements/fda-authorizes-booster-dose-pfizer-biontech-covid-19-vaccine-certain-populations> (last accessed 20 January 2021).
3. McMahon DE, Amerson E, Rosenbach M, Lipoff JB, Moustafa D, Tyagi A, Desai SR, French LE, Lim HW, Thiers BH, Hruza GJ, Blumenthal KG, Fox LP, Freeman EE. Cutaneous reactions reported after Moderna and Pfizer COVID-19 vaccination: A registry-based study of 414 cases. *J Am Acad Dermatol*. 2021; **85**(1):46-55.
4. Robinson LB, Fu X, Hashimoto D, Wickner P, Shenoy ES, Landman AB, Blumenthal KG. Incidence of Cutaneous Reactions After Messenger RNA COVID-19 Vaccines. *JAMA Dermatol*. 2021 Aug 1;157(8):1000-1002. doi: 10.1001/jamadermatol.2021.2114. PMID: 34160555; PMCID: PMC8223130.
5. Blumenthal KG, Freeman EE, Saff RR, Robinson LB, Wolfson AR, Foreman RK, Hashimoto D, Banerji A, Li L, Anvari S, Shenoy ES. Delayed Large Local Reactions to mRNA-1273 Vaccine against SARS-CoV-2. *N Engl J Med*. 2021 Apr 1;384(13):1273-1277. doi: 10.1056/NEJMc2102131. Epub 2021 Mar 3. PMID: 33657292; PMCID: PMC7944952.

101 **Table 1.** “Morphologies of Cutaneous Booster Reactions to COVID-19 Vaccine Reported to the AAD/ILDS Registry”

	Number of Total Booster Reactions, regardless of whether patients reacted to prior vaccine doses (total individuals = 36, total number of distinct reactions = 93)						Subset Analysis: Number of Booster Reactions, limited to patients who only reacted to booster, and not to prior vaccine doses (total individuals = 26, total number of distinct reactions= 71)	
Morphology*	Total		Moderna		Pfizer		Total	
	n	% of total reactions	n	% of total reactions	n	% of total reactions	n	% of total reactions (restricted to individuals who only reacted to booster dose)
Urticaria	14	15.1%	10	10.8%	2	2.2%	12	16.9%
Localized swelling	11	11.8%	7	7.5%	2	2.2%	9	12.7%
Localized redness	13	14.0%	9	9.7%	2	2.2%	11	15.5%
Localized pain	11	11.8%	7	7.5%	2	2.2%	9	12.7%
Pruritus	10	10.8%	8	8.6%	2	2.2%	7	9.9%
Delayed hypersensitivity	9	9.7%	8	8.6%	1	1.1%	6	8.5%
Morbilliform	3	3.2%	1	1.1%	2	2.2%	2	2.8%
Vesicular	3	3.2%	2	2.2%	1	1.1%	2	2.8%
Erythromelalgia	3	3.2%	3	3.2%	0	0.0%	2	2.8%
Contact dermatitis	2	2.2%	1	1.1%	1	1.1%	1	1.1%
Angioedema	2	2.2%	1	1.1%	1	1.1%	2	2.8%
Pernio/Chilblains	1	1.1%	0	0.0%	1	1.1%	0	0.0%
Livedo reticularis	1	1.1%	1	1.1%	0	0.0%	1	1.1%
Erythema multiforme	1	1.1%	1	1.1%	0	0.0%	1	1.1%
Pityriasis rosea	1	1.1%	0	0.0%	1	1.1%	1	1.1%
Flare of an existing condition	1	1.1%	1	1.1%	0	0.0%	0	0.0%
Other	7	7.5%	3	3.2%	2	2.2%	5	7.0%

102 *Listed as number of reactions. Individual person may have more than one reaction.